

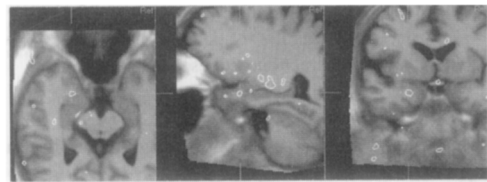
## High Resolution Free Form Deformation Analysis of Atrophy from Longitudinal MRI Studies of Mild Cognitive Impairment.

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A fraction of elderly subjects are found to have some form of mild cognitive impairments, especially memory deficits, on neuropsychological testing. These patients are believed to be at a higher risk to develop the clinical criteria of Alzheimer's dementia, than non-impaired elderly. It is thought that many subjects with mild cognitive impairment have an early form of Alzheimer's disease. To test for associated structural changes in the brain, a group of six subjects, who were diagnosed with mild cognitive impairment according to Mayo Clinic criteria, were imaged using sequential anatomical MRI acquisitions[1]. Two images were acquired on each subject, between 1 and 5 years apart, using a high-resolution 3D MPRAGE acquisition(1x1x1.5mm) on a 1.5T Siemens system. A group of 14 age matched control subjects were scanned over similar time periods to form an age-atrophy reference. An additional age matched normal was used as a reference MRI anatomy for the analysis.

A high-resolution free form registration algorithm was used[2] to estimate a fine Cubic B-Spline deformation mapping each subject's first time point scan into the coordinates of the reference MRI. An hierarchical multi-grid deformation refinement scheme was used, with the finest deformation lattice spacing set to 2.4mm. A single level (2.4mm spacing) version of this registration procedure was then used to estimate the deformation between each subjects two longitudinal acquisitions. The point wise volume change was estimated analytically at each voxel location from the B-Spline model of the deformation, to create an atrophy map in the coordinate system of the first time point scan of each subject. Using the transformation to the reference atlas, each atrophy map was then transformed to the common reference anatomy coordinates. Two statistical maps were then created, one for the normal control group and one for the M.C.I. group. These consisted of the mean and standard deviation of the normalised annual point wise volume change at each voxel. The voxels with significantly different atrophy rates were then evaluated based on the Z-Score of the statistics at each voxel in the two groups.



**Figure 1:** Average Normal MRI with overlay of iso Z-score contour ( $Z=1.6$ ) showing the common regions of loss in the MCI group with respect to the normal group.

Significant decreases in tissue volume from normal to MCI group are illustrated in figure 1, showing the average normal MRI, with a Z-Score contour( $Z=1.6$ ) of the volume changes overlaid. Decreases were observed in white matter around the ventricles and in gray matter at the head of the hippocampus, a region which is known to be particularly vulnerable to Alzheimer's disease. In addition, smaller regions of loss were observed in the gray matter of the cortex. Overall, the results demonstrate that mild cognitive impairment is associated with increased rates of brain atrophy in regions that are known to be involved in Alzheimer's disease. Additional studies are necessary to determine the diagnostic value of these atrophy measurements for the early diagnosis of Alzheimer's disease.

### References

- [1] NC. Fox, EK. Warrington, MN. Rossor, Serial magnetic resonance imaging of cerebral atrophy in preclinical Alzheimer's disease, *Lancet* 1999;353:2125
- [2] C. Studholme, V. Cardenas, M.W. Weiner, Multi Scale Image and Multi Scale Deformation Based Registration of Brain Anatomy for Building Average Brain Atlases, *Proc. SPIE Medical Imaging*:2001.